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Institution:

Central Park Teaching Hospital

**SYNOPSIS OF RESEARCH ARTICLE FOR FCPS–II IN
PEDIATRIC MEDICINE**

**COMPARISON OF THE CLINICAL EFFICACY OF BACTERIA-BASED
PROBIOTICS TO FUNGI-BASED PROBIOTICS IN ACUTE WATERY
DIARRHEA IN PEDIATRIC OUT PATIENT DEPARTMENT**

BY

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INTRODUCTION:

Diarrhea is one of the leading causes of death in developing countries. Lack of adequate hygiene, sanitation, and unavailability of clean drinking water are the leading causes of Acute Watery Diarrhea in developing countries. Etiology of diarrhea is mainly viral (rotavirus), bacterial (*Escherichia coli*), and parasitic infections, but may also be due to drug therapy, malnutrition, food allergies, and gastrointestinal disorders.⁽¹⁾ As per the World Health Organization (WHO) and UNICEF, about 1.9 million children younger than 5 years die from diarrhea each year, mainly in developing countries. This contributes to 18% of all the deaths of children <5 years and >5000 children are dying every day. For such demises, majority as 78% take place in African and Southeast Asian regions.⁽²⁾ Complications associated with acute watery diarrhea include prolongation of diarrheal episodes leading to malnutrition, secondary infections and micronutrient deficiencies.⁽³⁾ Probiotics are recommended to use in childhood diarrhea, childhood allergies, antibiotic associated diarrheas, inflammatory bowel disease and irritable bowel syndrome.⁽⁴⁾

A randomized clinical trial conducted in Iran compared the efficacy of bacterial and fungal probiotics, and found bacterial probiotic i.e. *Lactobacillus* to be superior to fungal probiotic i.e. *Saccharomyces boulardii* in which they reported that the mean diarrhea rate before 24 hours greatest in fungal group (2.10 days) followed by the placebo group (1.90 days) and bacterial probiotics (1.73 days). The median duration of diarrhea from onset of treatment to recovery was longest for placebo group (4.43 days) then fungal probiotics (3.17 days) and was the shortest for bacterial probiotics (2.80 days). The mean duration of diarrhea before admission was in the bacterial probiotic (6.63 days), placebo group (6.17 days) and in the fungal probiotic (6.03 days).⁽⁵⁾ An open label randomized control trial conducted in India compared the efficacy of *Saccharomyces boulardii*, *Bacillus clausii*, and *Lactobacillus rhamnosus* GG preparation in the treatment of acute diarrhea in children, and concluded that *Lactobacillus rhamnosus* (87.5%) was superior to *Bacillus clausii* (67.5%) followed by *Saccharomyces boulardii* (65%) for the improvement of Group A received *S. boulardii*, Group B received *B. clausii* and Group C received *L. rhamnosus* GG. groups according to improvement/persistence of stool ($p=0.045$). Most of the cases (49.17%) were observed in age group 5 to 10 followed by <5 years of age (Chi-square=6.844 with degree of freedom; $p=0.335$). Initially all cases were observed with liquid stool, then on day 2 and day 3 there was statistically significant improvement in consistency was observed in Group C as compared to Group A and Group B ($p<0.001$).⁽²⁾ A similar study conducted in Pakistan that compared the efficacy of bacterial vs fungal probiotics, and were of the conclusion that clinical efficacy of bacteria-based probiotics, i.e. *Lactobacillus acidophilus* is higher than fungi-based probiotics, i.e. *Saccharomyces boulardii* in the treatment of acute watery diarrhea. Comparison of efficacy in both groups showed that diarrhea was resolved in 57.33% in group A and 28% in group B while the rest of 42.67% in group A and 72% in group B did not show efficacy. A statistically significant difference ($p\text{-value}=0.0001$) was found in the comparison of the efficacy of both groups. Frequency & severity of acute diarrhea was equal in both genders i.e. 52% in group A and 58.67% in group B affected by diarrhea were males, while 48% in group A and 41.33% in group B affected by diarrhea were

females. Both bacterial and fungal probiotics showed significant clinical efficacy in diarrhea treatment.⁽⁶⁾

This study is planning to compare the clinical efficacy of bacterial versus fungal probiotic in acute watery diarrhea. A clear consensus has not been reached regarding the use of appropriate probiotic. Some pediatricians are of the opinion that bacterial probiotic are superior to fungal probiotics along with rehydration for improvement of diarrhea. However, others experience is that fungal probiotics are better along with rehydration for the improvement of diarrhea. A high-quality evidence basis must be established that guides the pediatrician regarding the choice of probiotic. The results of this study will help guide pediatricians to the better probiotic for the clinical improvement of acute diarrhea in our setup.

OBJECTIVES:

To compare the clinical efficacy of bacteria-based probiotics to fungi-based probiotics in acute watery diarrhea in pediatric out patient department.

OPERATIONAL DEFINITION:

Acute Watery Diarrhea: It is defined as defecation frequency >3 times / day for less than 14 days and fecal characteristics in accordance with Bristol fecal characteristics types 6 and 7. (Annexure 1)

Probiotic: It is defined as live microorganisms, that when administered in adequate amounts, confer a health benefit on them.

Efficacy: It is defined as a patient having less than ≤ 3 episodes of stool with Bristol grade 5 or less on the third day.

MATERIALS & METHODS:

Setting: Department of Pediatric Medicine, Central Park Teaching Hospital, Lahore.

Study design: Randomized Control Trial

Study duration: Six months after approval of synopsis.

Sample size: A sample size of 86 (43 in each group) is calculated using Open Epi tool at 5% level of significance and 80% power of test, and taking expected rate of 57.33% resolution of diarrhea with bacterial probiotic and diarrhea resolution rate of 28% with fungal probiotic after 3 days.⁽⁶⁾

Sampling technique: Non probability consecutive sampling

SAMPLE SELECTION

Inclusion criteria

1. Children aged 0 to 59 months
2. Acute Watery Diarrhea
3. The child's parents or caregiver understands, agrees to participate, and complies with the study protocol

Exclusion criteria

1. Patients with bloody diarrhea, severe dehydration, severe electrolyte imbalance, immunocompromised children, or malabsorption disorders and systemic illnesses (sepsis, pneumonia, urinary infections)
2. Those who have already used antibiotics or probiotics during this illness
3. Known hypersensitivity to probiotics

DATA COLLECTION PROCEDURE

Patients fulfilling the inclusion criteria, presenting in the Pediatric Out patient department, Central Park Teaching Hospital, Lahore will be enrolled in the study. Written informed consent will be taken from all patients' guardian. Patients will be randomly divided into two groups using opaque envelope method. Group A patients will be treated with bacterial probiotic, i.e *Bacillus clausii* 2 billion spores given twice daily and group B will be treated with fungal probiotic, i.e *Sacchromyces boulardii* 250mg twice daily, in addition to standard diarrheal treatment. The patients will be followed at 3rd day to assess improvement in diarrhea. If the patient had ≤ 3 episodes of stool with Bristol grade 5 or less it was considered as a positive outcome.

DATA ANALYSIS

Data will be entered and analyzed by using SPSS version 21. Mean $\pm$ SD will be calculated for age. Frequency and percentages will be calculated for gender. Grade and frequency of stool will be noted. Both groups will be compared for efficacy of bacteria-based probiotics to fungi-based probiotics in acute watery diarrhea in paediatric out patient department using chi-square test taking p-value of less than or equal to 0.05 as significant after 3 days of treatment. Data will be stratified for age, gender and grade and frequency of stool. Post stratification chi-square test will be used taking p-value of less than or equal to 0.05 as significant.

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1. Syed M, Gondi S, D V, P U. Study on efficacy of probiotic use in pediatric acute diarrhea: A prospective open-labeled study. *Natl J Physiol Pharm Pharmacol*. 2023;14(5):1.
2. Sharma AK, Puri N, Mathur M, Mathur A. A randomized controll trial to compare the efficacy of saccharomyces boulardii, bacillus clausii, and lactobacillus rhamnosus GG preparation in the treatment of acute diarrhea in children. *Asian J Pharm Clin Res*. 2022 Mar 14;63–7.
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5. Sharif A, Ardakani AT, Kashani HH, Rabiee F, Sharif MR. Comparison Efficacy of Bacterial and Fungal Probiotics on Acute Pediatric Diarrhea A Randomized Clinical Trial [Internet]. 2019 [cited 2024 Sept 3]. Available from: <https://www.researchsquare.com/article/rs-2183/v1>
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Annexure-1

BRISTOL STOOL CHART		
TYPE 1		Separate hard lumps VERY CONSTIPATED
TYPE 2		Lumpy and sausage like SLIGHTLY CONSTIPATED
TYPE 3		A sausage shape with cracks in the surface NORMAL
TYPE 4		Like a smooth, soft sausage or snake NORMAL
TYPE 5		Soft blobs with clear-cut edges LACKING FIBER
TYPE 6		Mushy consistency with ragged edges INFLAMMATION
TYPE 7		Liquid consistency with no solid pieces INFLAMMATION AND DIARRHEA

PROFORMA

**COMPARISON OF THE CLINICAL EFFICACY OF BACTERIA-BASED
PROBIOTICS TO FUNGI-BASED PROBIOTICS IN ACUTE WATERY
DIARRHEA IN PEDIATRIC OUT PATIENT DEPARTMENT**

Age: _____

Gender: _____

Registration #: _____

Group

A ☐

B ☐

Bristol score on day of presentation: _____

Frequency of stool on day of presentation: _____

Bristol score on 3rd day

Bristol 5 or less ☐

Bristol 5 or more ☐

Frequency of stool on 3rd day

Less than 3 ☐

More 3 ☐

Outcome:

Positive ☐

Negative ☐

Informed Consent Information

Title of the Study

Comparison of the Clinical Efficacy of Bacteria-Based Probiotics and Fungi-Based Probiotics in Acute Watery Diarrhea in Children in the Pediatric Outpatient Department

Principal Investigator

Dr. Syeda Sabeen Fatima Naqvi

Pediatric Medicine

Central Park Teaching Hospital, Lahore

Phone: 03027558817

Email: syedasabeen2015@gmail.com

Purpose of the Study

You are being asked to participate in this research study. Before deciding whether to participate in this study, it is important that you understand why the research is being conducted and what your participation will involve. Please read the following information carefully. If anything is unclear or if you need further information, please ask the principal investigator.

The purpose of this study is to **compare the clinical efficacy of bacteria-based probiotics and fungi-based probiotics in acute watery diarrhea in children in the pediatric outpatient department**. The results of this study will help our pediatricians in determining which probiotic is better for the clinical improvement of acute diarrhea.

Study Procedure

This is an experimental study being conducted on children who present with acute watery diarrhea in the pediatric outpatient department. The patients will be randomly divided into two groups by the lottery method. One group will receive a bacterial probiotic and the other group will receive a fungal probiotic. In addition to the standard treatment for diarrhea, the child will be given the required number of probiotic doses. The number and consistency of stools will be recorded. The duration of the study is **6 months**.

Risks

There are **no specific risks identified**.

You may ask any questions and may seek clarification at any time. You can also discuss any concerns with the principal investigator.

Benefits

There is **no direct benefit** to you from participating in this study. However, it is hoped that the information obtained from this study will help pediatricians in the future to provide better clinical management of children with acute diarrhea and to select the better probiotic.

Confidentiality

The principal investigator will keep your identity confidential for the purposes of this research study. Every effort will be made to maintain confidentiality.

- You will be assigned a **code number/name** for the purpose of the study, and all research notes and documents will be identified using this code.
- Your name, identity, and other personal information will be kept in a **locked file cabinet** and will not be disclosed to anyone.

The principal investigator will report the study results. In particular, any incidents that are legally required to be reported will be reported to the relevant authorities.

Contact Information

If you have any questions regarding this study, you may contact me. If you experience any adverse effects as a result of participating in this study, you may contact the principal investigator through the contact information provided on the first page.

If you have any questions regarding your rights as a research participant, or if you face any problem that cannot be discussed with the principal investigator, you may contact the **Research Ethics Committee**.

Voluntary Participation / Withdrawal from the Study

Participation in this study is entirely voluntary. You may choose whether or not to participate in the study.

If you decide to participate in this study and subsequently wish to withdraw, you may do so at any time without giving any reason and without affecting your right to receive appropriate medical care.

If you withdraw from the study, the information already collected from you may still be used for the purposes of this research, as permitted by the study requirements.

You will not lose any benefits to which you are otherwise entitled if you decide not to participate or if you withdraw from the study.

Consent

I have been provided with the information about this study and have understood it. I understand that I have the opportunity to ask questions. I understand that my participation in this study is voluntary and that I may withdraw from the study at any time without giving any reason and without affecting my medical care.

I have understood the information provided to me and agree to participate in this study.

Signature of Participant: _____

Date: _____

Signature of Principal Investigator: _____

Date: _____

CPMC/IRB-No/1503

September 27, 2024

INSTITUTIONAL ETHICAL & REVIEW BOARD

Project: "Comparison of the clinical efficacy of bacteria based probiotics to fungi based probiotics in acute watery diarrhea in pediatric out patient department"

Principal Investigator(s): Dr. Syeda Sabeen Fatima Naqvi

Department(s): Department of Pediatric Medicine, Central Park Medical College & Teaching Hospital, Lahore

Date considered: September 17, 2024

Date approved: September 23, 2024

This ethical approval is for six months. Any change in the protocol or further extension in the period of study should be notified to the committee for prior approval.

Chairman IRB: _____

Prof. Muhammad Amer Mian
MBBS, FCPS, CHPE
Chairman IRB
Central Park Medical College, Lahore
chairmanirb@cpmc.edu.pk

This ethical approval is issued subject to the following conditions:

1. A signed personal declaration of responsibility.
2. If the research question changes significantly so as to alter the nature of the study, a new application for ethical clearance must be submitted.
3. It remains the principal investigator's responsibility to ensure that all the necessary forms and informed consent are retained for future reference.

**Please quote the IRB approval number in all inquiries.*